REMARKS

The invention

The invention features E4orf4-encoding nucleic acids, pharmaceutical compositions, and expression vectors containing the same, and methods for their use.

Claims at issue

Claim 81, from which claims 85-87 depend, is directed to a method of inducing apoptosis of a cell. According to this method, the intratumoral administration of a nucleic acid encoding a polypeptide containing a sequence of SEQ ID NO: 4 results in the induction of apoptosis upon expression in a cell.

Claim 95, from which claims 99 and 100 depend, is directed to an expression vector encoding an E4orf4 polypeptide (containing the sequence of SEQ ID NO: 4) and capable of inducing apoptosis. Claim 88, from which claims 92 and 93 depend, is drawn to a pharmaceutical composition containing such an expression vector.

The Office action

Claims 81, 85-88, 92, 93, 95, 99, and 100 are pending. Claims 81 and 85-87 are in condition of allowance. Claims 88, 92, 93, 95, 99, and 100 stand rejected under 35 U.S.C. § 112, first paragraph, and under 35 U.S.C. § 102(e). Each of these rejections is addressed below.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 88, 92, 93, 95, 99, and 100 stand rejected under 35 U.S.C. § 112, first paragraph, as containing an inadequate written description. In applying this rejection, the Examiner asserts that the phrase "wherein E4 polypeptides other than said E4orf4 polypeptide are not expressed by said vector" in amended claims 88 and 95 is considered new matter because the specification fails to sufficiently describe vectors which express no E4 polypeptides other than E4orf4. Applicants respectfully traverse this rejection.

M.P.E.P. § 2163 IB states "While there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure." Applicants submit that the present specification provides ample support for a vector which expresses an E4orf4 polypeptide in the absence of any other E4 polypeptides. As a specific example, Applicants direct the Examiner to Fig. 12, which shows the infection of SAOS cells with an adenoviral vector (Ad5) encoding *only the E4orf4 protein* (dl 1014). In particular, the specification states at page 30, lines 19-22 (emphasis added):

> Further Trypan Blue™ exclusion experiments on Saos-2 cells following infection with mutants *dl*1014, *which expresses E4orf4 only*, *dl*1015, which expresses E4orf4 and E4orf3, *dl*1011, which expresses no E4 products, as well as mock-infected cells, were conducted.

Similarly, the studies depicted in Figures 13 and 14 employ plasmids encoding various E4 products (E4orf1, E4orf2, E4orf3, E4orf4, or E4orf6) each of which contains a

single E4 product. In these experiments, each of the E4 product was generated by subcloning the cDNA sequence encoding the protein product of *individual* E4orfs (E4orf1-6) into the pcDNA3.1 expression plasmid (see, for example, page 22, lines 20-22 and page 31, lines 5-11 and lines 17-21). For example, page 18, lines 2-6 of the specification states (emphasis added):

> Fig. 14 is a graph showing that *E4orf4* and E4orf6, when expressed *individually* or together with luciferase by transient transfection of an E4orf4- or an E4orf6-encoding plasmid induces cytotoxicity in p53-null cells, as judged by the low expression of a co-transfected reporter plasmid encoding luciferase, relative to non-cytotoxic inducing control plasmids encoding E4orf1, E4orf2, and E4orf3.

Based on the above teachings, Applicants submit that the specification clearly provides numerous examples of vectors expressing the E4orf4 polypeptide in the absence of any other E4 polypeptides and therefore contains an adequate written description for such vectors. Because the M.P.E.P. § 2163.02 states "[t]he subject matter of the claim need not be described literally (i.e. using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement," the inclusion of the phrase "wherein E4 polypeptides other than said E4orf4 polypeptide are not expressed by said vector" in claims 88 and 95 does not represent new matter. Accordingly, the § 112, first paragraph rejection should be withdrawn.

Rejection under 35 U.S.C. § 102(e)

Claims 88, 92, 93, 95, 99, and 100 stand rejected under 35 U.S.C. § 102(e) as

being anticipated by Kaplan *et al.* (U.S.P.N. 6,100,086; hereafter "Kaplan"). In particular, the Examiner states that Kaplan, in disclosing an Ad2 vector containing an E4orf4 transgene inserted into the Ad2-βgal-7 vector (after removing the β-galactosidase gene) in a buffer solution (considered to be a pharmaceutically acceptable carrier), anticipates the present claims. Applicants respectfully traverse this rejection.

The Kaplan reference is not prior art to the present application, which claims an earlier priority date. While Kaplan's application was filed on April 14, 1997, the instant application claims priority from U.S. provisional application No. 60/028,740 (hereafter the '740 application), filed on October 22, 1996.

As stated above, the present invention features methods and compositions relating to E4orf4-encoding nucleic acids. Support for the claimed invention can be found throughout the '740 specification, from which the present application claims priority. For example, Applicants direct the Examiner to figures 12 and 13 of the '740 application that are identical to figures 12 and 13 of the present application and that clearly show that expression of E4orf4 in the absence of any other E4 polypeptide results in the induction of apoptosis. Thus, these disclosures in the '740 application are identical to those of the present application.

Given that the claimed invention is fully supported by the '740 application, the present claims have an effective priority date of October 22, 1996. Consequently, Kaplan, which has an earliest priority date of April 14, 1997, is not prior art and therefore cannot be

considered anticipatory to the present invention. Applicants therefore respectfully request that the § 102(e) rejection be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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